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EPIDEMIOLOGY IN RISK ASSESSMENT FOR REGULATORY POLICY

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"The uncharted galaxies of epidemiology are numerous"
Lilienfeld *et al.* [11]

I. INTRODUCTION

THE TWENTIETH century has seen the rapid evolution of many new fields concerned with protecting public health. Epidemiology and risk assessment have several of the features common to these new fields, and important differences. Both are needed to make the difficult decisions required in setting standards for levels of toxic agents in the workplace and environment. They differ in their aims, orientation, and time scale.

According to Lilienfeld and Lilienfeld [2], epidemiology is "the study of the *distribution of a disease* or a physiological condition in human populations and of the factors that influence this distribution" (italics added). By contrast, health risk assessment denotes research and evaluation to characterize the probability of physical harm to humans attributable to a *particular agent or group of agents*. While the distribution of disease provides the focus for epidemiologic research, concern for adverse effects of specific toxicants drives risk assessment. Moreover, while epidemiologic studies proceed at the glacier-like pace needed to mobilize large staffs of support personnel and to monitor large populations over long periods of time, risk assessment activities acquire the urgency felt by regulators, who must make decisions (including decisions to postpone decisions) today. Most important, while epidemiology is a scientific field that draws upon medicine, demography, and statistics, risk assessment is a hybrid of science and policy that draws not only upon fields such as epidemiology, toxicology, chemistry and engineering, but also upon psychology, politics, economics, law and social justice.

These inherent differences in emphasis, timing, and nature complicate the role played by epidemiology in risk assessment for regulatory policy. In 1985, this role is still largely one of epidemiology's uncharted galaxies. In the sections below, I review the role's history, and the reasons why it will continue to play an essential part in regulatory decision-making. The role has placed epidemiologic findings and epidemiologists at the center of political controversies, and I discuss the positive and negative side effects of this new visibility. Finally, I explore ways to prevent the negative side effects and ways to increase the utility of epidemiologic data for regulatory risk assessment.

II. THE ROLE OF EPIDEMIOLOGY IN RISK ASSESSMENT

Concern about industrially related contaminants in our air, water, and food began gathering momentum shortly before World War II, and accelerated with the publication in 1963 of Rachel Carson's book, **The Silent Spring**. The spectre she painted of man's

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TABLE 1. PARTIAL LIST OF FEDERAL LEGISLATION REGULATING TOXIC SUBSTANCES

Legislation	Year passed
Delaney Clause of Food, Drug and Cosmetic Act	1959
Federal Hazardous Substances Act	1960
Clean Air Act	1970
Occupational Safety and Health Act	1970
Consumer Product Safety Act	1972
Federal Environmental Pesticide Control Act	1972
Federal Insecticide, Fungicide and Rodenticide Act	1972
Safe Drinking Water Act	1974
Resource Conservation and Recovery Act	1976
Toxic Substances Control Act	1976
Clean Water Act	1977

TABLE 2. FEDERAL AGENCIES REGULATING TOXIC SUBSTANCES

Agency	Year established
Food and Drug Administration	1928
Environmental Protection Agency	1970
Occupational Safety and Health Administration	1970
Consumer Product Safety Commission	1972

TABLE 3. FEDERAL RESEARCH ORGANIZATIONS INVESTIGATING TOXIC SUBSTANCES

Organization	Year established
National Cancer Institute	1937
National Institute for Environmental Health Sciences	1969
National Institute for Occupational Safety and Health	1971
National Toxicology Program	1978

destruction of the earth with industrial emissions fueled public pressure for a rash of environmental legislation, some of which is listed in Table 1. Tables 2 and 3 show the parallel evolution of federal agencies created by Congress to regulate and control toxic emissions, and of federal research institutes to provide the scientific basis for such regulation. These developments have led many to regard the 1970's as "the decade of the environment". Although motivation for the environmental movement included concern about the adverse effects of contaminants on respiratory function, reproductive outcomes and genetic mutations, the most compelling constituent was public fear that the global destruction predicted by Carson would include an epidemic of chemically induced cancers.

Figure 1 shows temporal trends in the estimated probability that a white male baby born in the U.S. will either develop cancer or die from it. The temporal increase does not reflect the feared epidemic. Rather it reflects the greater proportion of men who will survive to old age when cancer risks are highest, as well as the more accurate diagnoses among the elderly, and the effects of tobacco. Apart from this real increase in cancer incidence and mortality, there is a perceived one due to the openness with which the disease is now

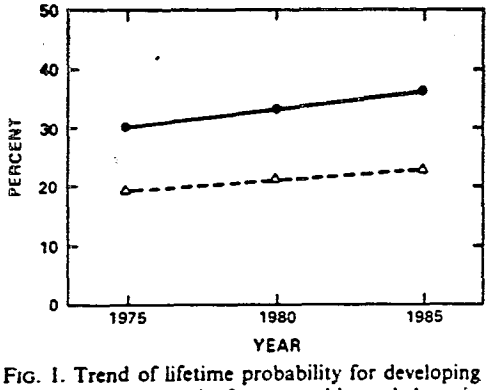

FIG. 1. Trend of lifetime probability for developing (——) or dying (– – –) of cancer, white male born in the United States. (Source [3]).

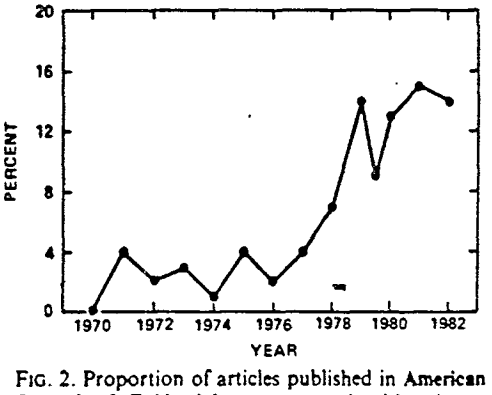

FIG. 2. Proportion of articles published in American Journal of Epidemiology concerned with adverse health effects of physical and chemical agents in the workplace or general environment.

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discussed. It is unthinkable today that a U.S. President would undergo furtive oral cancer surgery on a yacht in New York's East River to keep it from his constituents, as did Grover Cleveland in 1893.

The environmental movement of the 1970's has had a direct impact on the substance of epidemiologic studies. Figure 2 shows the increase with time in the proportion of those articles in the **American Journal of Epidemiology** that are devoted to the adverse effects of physical and chemical agents in the workplace and environment. Although a sizable part of this new research has examined acute and chronic respiratory disorders and reproductive disorders, the largest portion has dealt with environmentally and occupationally induced cancer. That cancer should monopolize a disproportionate share of the research reflects patterns of research funding, which in turn reflect priority patterns of public fear. Many of the examples and much of the discussion in this paper concern the relationship between epidemiology and risk assessment for cancer, although the problems and future prospects apply to other diseases as well.

Estimating risks to health from environmental agents using human data must proceed in the face of formidable obstacles. Most toxic exposures occur chronically at levels that are low, variable, and measured with substantial error. Epidemiologic studies are likely to overlook a large number of small effects associated with such exposures. Data from those occupational studies dealing with high exposures and large effects typically provide limited guidance about risks at low environmental levels, as can be seen by comparing the very high lung cancer death rates of U.S. uranium miners with those of smoking and nonsmoking U.S. veterans, shown in Fig. 3. An individual living in the U.S. today inhales naturally occurring radon gas and its radioactive decay products at an average rate of roughly two-tenths of a WLM per year [6]. (A WLM, the acronym for "working-level-month", is a unit of cumulative exposure to α-radiation.) By age 70 he will have inhaled a total of about 14 WLM, a small amount in comparison with totals in excess of 3000 WLM inhaled by U.S. uranium miners before the establishment of a federal standard in 1970. The startling excess of lung cancer among these miners relative to that of other U.S. white males illustrates the difficulty in attempting to use these data to estimate risks from low levels of radiation.

The difficulty is also evident upon examination of the standardized mortality ratios (SMR's) shown in Fig. 4. The SMR's were computed using the entire cohort as the standard, and were normalized so that miners in the lowest exposure category of 0–21 WLM form the referent group. Interest centers on risk among miners in the 22–119 WLM range, because these exposures approximate those experienced by individuals living in areas with very high background radon levels. However, the evidence is equivocal: although the death rate for the 22–119 WLM group is almost twice that of the referent group, the increase is not statistically significant at the 5% level.

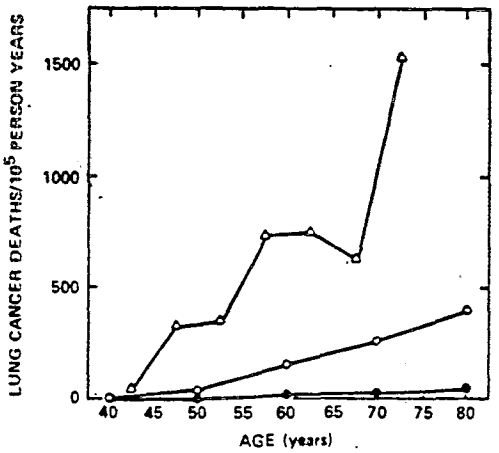

FIG. 3. Age-specific lung cancer mortality rates in U.S. uranium miners (△——△), smoking U.S. veterans (○——○) and non-smoking U.S. veterans (●——●). (Source [4, 5].)

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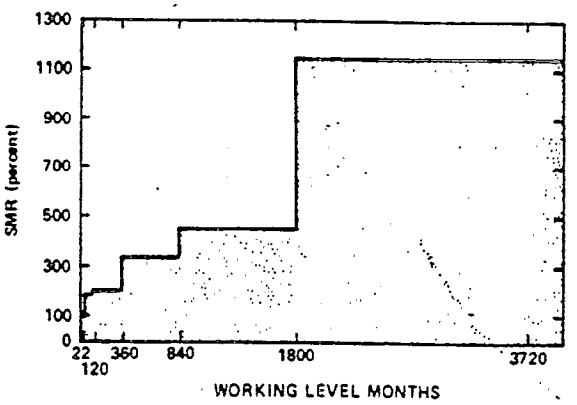

FIG. 4. Standardized mortality ratios (SMRs) for lung cancer by working-level-months (WLM) of cumulative exposure in United States uranium miners. SMRs were normalized to 100% for exposure category 0–21 WLM. (Source [4]).

Monitoring populations for disease is time-consuming, expensive, and vulnerable to serious bias. One must worry that comparisons between exposed and unexposed populations are not confounded by differences in smoking and other determinants of health, nor biased by differences in subjective assessments of disease. Such worries are aggravated in studies of environmentally induced disease, because the effects are likely to be small and the danger of reporting bias great.

These obstacles do not vitiate the strengths of epidemiology in risk assessment for regulatory policy. As noted by Doll in the context of policy-setting for the prevention of cancer [7], human observations continue to make several essential contributions to risk assessment. In the paragraphs below I list some of the reasons why human data are needed for regulatory decisions.

First, they are needed to detect unsuspected hazards that have not emerged from laboratory tests. Animal experiments are still imperfect tools for detecting human cancer, largely because of the great variability across species in response to chemicals, and our lack of understanding about the causes of this variability. The International Agency for Research on Cancer has determined that there is sufficient evidence from human observations, but limited, inadequate, or nonexistent evidence from animal experiments, to classify as carcinogens the chemicals or chemical processes listed in Table 4. The fact that most of these chemicals have tested positive in one or more of the short-term *in vitro* or *in vivo* tests now in use, reflects not the sensitivity of the test battery but rather the intense scrutiny the chemicals have received, relative to those for which no human data are available. Moreover, the tests are not specific; one or more of them have been positive for a vast number of chemicals occurring naturally in the foods we eat and the products we use. Thus laboratory tests do not yet provide a reliable screen for human carcinogens, and they are of limited or no utility for many other diseases or conditions associated with environmental exposures. Human data will continue to be needed, despite the obvious desirability of discovering health hazards before human exposure to them.

Second, human data are needed to estimate exposure levels producing the highest additional risk that is socially acceptable. Just as laboratory tests provide imperfect screens

TABLE 4. CHEMICALS OR INDUSTRIAL PROCESSES WITH SUFFICIENT* EVIDENCE FOR CARCINOGENICITY IN HUMANS BUT NOT IN EXPERIMENTAL ANIMALS†

Arsenic and certain arsenic compounds
Manufacture of auramine
Benzene
N,N-bis(2-cholorethyl)-2-naphthylamine (chlornaphazine)
Undergroud mining of hematite
Manufacture of isopropyl alcohol (strong acid process)
Mustard gas
Nickel refining

*As defined by the International Agency for Research on Cancer [8].
†Source: [8].

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TABLE 5. ESTIMATED HUMAN BLADDER CANCER RISKS (CANCERS/10^6 POPULATION) FOR LIFETIME SACCHARIN INGESTION OF 0.12 G/DAY*

Interspecies extrapolation method	Low dose extrapolation method			
	Single-hit	Multistage	Multihit	Probit
Body surface area	1200	5	0.001	450
mg/kg/day	210	—	0.001	21
mg/kg/lifetime	5200	—	0.001	4200

*Extrapolated from Rat Bladder Tumor Data. Source [9].

TABLE 6. RISK OF BLADDER CANCER AMONG USERS OF ARTIFICIAL SWEETENERS RELATIVE TO RISK AMONG NONUSERS (ESTIMATED FROM CASE–CONTROL STUDIES)

Authors	Males	Females
Hoover *et al.* [10]	0.99	1.00
Kessler and Clark [11]	0.97	1.01

for potential toxicants, so also are they extremely limited tools for obtaining quantitative estimates of risk. Table 5 shows that estimates of human bladder cancer risk associated with saccharin, derived from a single positive experiment in laboratory rats, can differ by as much as six orders of magnitude, depending on the assumptions used to extrapolate across species and dose level. By contrast, the consistent lack of association found in six case-control studies of bladder cancer (see Table 6 for a sample) provide an upper bound on the actual level of human risk. Of course, neither human nor laboratory data can prove that a substance is harmless, but consistent negative findings in humans provide reassurance about the probable magnitude of the hazard.

Third, human data are needed to check inferences about a putative cause for a disease by monitoring the effect of its removal. Such checks require time, due to the long lag between exposure onset (or termination) and disease occurrence that is characteristic of many chronic diseases. For example, we can only now begin to monitor the effects on U.S. lung cancer rates of reductions in tar and nicotine content of cigarettes and in cigarette use since the 1950's. Figure 5 shows a modest but clear downward trend with year of birth in age-specific lung cancer death rates among young U.S. white males. Each successive birth cohort contains fewer men who started smoking, and among those who did, a higher proportion who smoked low tar cigarettes.

Finally, human data are needed to provide a sense of perspective about the magnitude of various hazards to health, in order to set priorities for the expenditure of public and

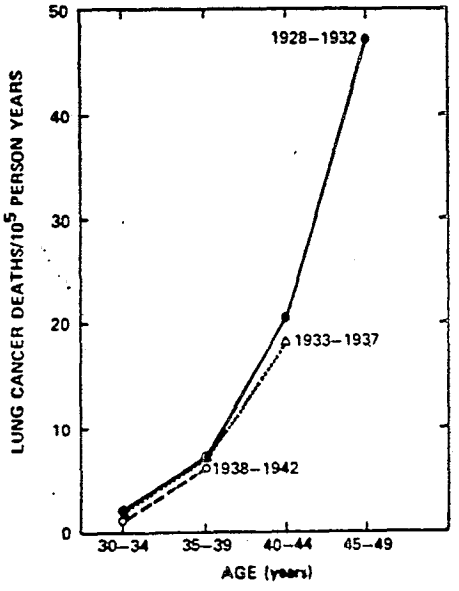

FIG. 5. Age-specific lung cancer mortality rates in United States white male cohorts. (Source [12].)

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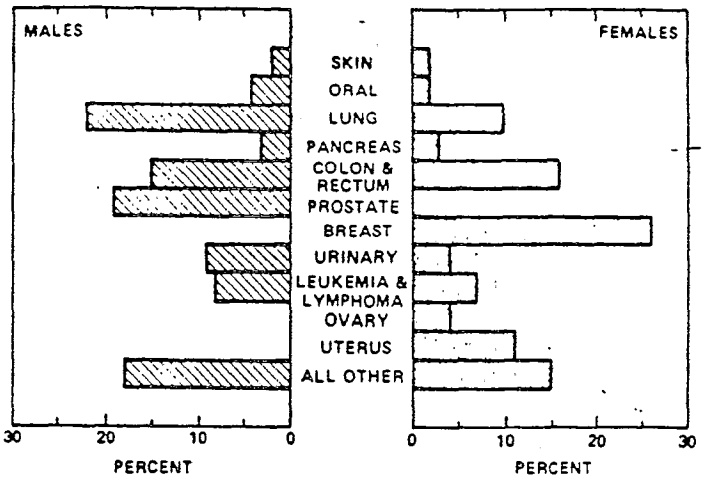

FIG. 6. Estimated percentage of all incident cancers occurring by site of origin in United States males or females in 1985, excluding nonmelanoma skin cancer and carcinoma *in situ*. (Source [13].)

private health resources so as to avoid spending disproportionate sums of money on minor hazards, while neglecting major ones. Figure 6 shows estimates of the percentage of all cancers diagnosed in the U.S. in 1985 occurring among the major sites, for men and women separately. Among men, cancers of the lung, large intestine and prostate account for about 56% of all new cancers (and 57% of all cancer deaths). Among women, cancers of the lung, large intestine and breast comprise 52% of all new cancers (and 51% of all cancer deaths). Table 7 shows that occupational and environmental factors do not play an appreciable role in the etiology of these major causes of morbidity and mortality, except for lung cancer. Moreover, the contribution to lung cancer is dwarfed by that of tobacco, which has been estimated to account for 91 and 79% of lung cancer deaths among U.S. men and women, respectively [14]. (The sum of the percentages for males exceeds 100% because of the multifactorial etiology of lung cancer.) To date, we have made slow progress in preventing cancers of the breast, prostate, and large intestine, which are more likely to

TABLE 7. ESTIMATED PERCENTAGES OF THE MAJOR SITE-SPECIFIC CANCERS ATTRIBUTABLE TO OCCUPATIONAL AND ENVIRONMENTAL FACTORS*

	Males	Females
Lung	15	5
Colon and rectum	2	1
Prostate	<1	—
Breast	—	0

*Source [14].

TABLE 8. BIOLOGICAL MARKERS FOR ENVIRONMENTAL EXPOSURES

Marker	Specimen	Methodology Refs
Chromosome aberrations (breaks, rearrangements, sister chromatid exchanges)	Blood lymphocytes, erythrocytes in bone marrow	Autoradiography, phytohemagglutinin stimulation of lymphocytes [33, 34]
Micronuclei	Erythrocytes in bone marrow	Microscopic examination [35]
Covalent binding to DNA	Blood lymphocytes, tissue explants	Radioactive labeling; immunoassays; indirect immunofluorescence microscopy [36]
Covalent binding to cellular proteins	Hemoglobin	Chromatography [37]
Cellular atypia	Sputum, cervical epithelium	Microscopic examination [38]
Mutagens	Urine, feces, cervical secretions, breast fluids	Ames salmonella test [39]
Sperm abnormalities	Semen	[40]

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kill us than are the pesticides we use to attack the insects in our homes. Such a perspective could help to assuage fear of cancer from environmental toxicants, and to direct the expenditure of public funds toward more cost-effective priorities.

III. THE IMPACT OF RISK ASSESSMENT ON EPIDEMIOLOGY

Clearly, epidemiologic observations continue to play an indispensable role in risk assessment for regulatory policy, and conversely, increasingly many epidemiologic studies are devoted to occupationally and environmentally induced disease. Increased public awareness of environmental issues and the need for risk assessment has brought epidemiology into courts, into homes on the evening news, and into leisure reading in the Sunday newspaper supplement. Thanks to such publicity, epidemiology is no longer an arcane word for an esoteric specialty. The need for epidemiology in risk assessment has brought employment opportunities and interesting scientific problems to epidemiologists. But it has also produced negative effects.

Problems arise because risk assessment is not a science, but rather a complex and often subtle fusion of facts and values. The problems are aggravated by the prevailing misconception that risk assessment for toxic substances is (or should be) entirely objective and scientific. This misconception is illustrated by the statement of the Office of Science and Technology Policy, Executive Office of the President, that toxic substance regulation consists of two stages: Stage I (risk assessment) uses empirical data and scientific judgement to characterize human exposure and risk; Stage II (policy) uses social and political action to decide regulatory action [5]. This separatist view is echoed by the National Academy of Sciences Committee on the Institutional Means for Assessment of Risks to Public Health, which reported:

> "We recommend that regulatory agencies take steps to establish and maintain a clear conceptual distinction between assessment of risks and consideration of the risk management alternatives; that is, the scientific findings and policy judgements embodied in risk assessments should be explicitly distinguished from the political, economic, and technical considerations that influence the design and choice of regulatory strategies" [16].

While it is useful to call attention to the desirability of such a distinction, I believe that in practice it is an unrealistic and unattainable goal. Values enter toxic risk assessment in many covert ways. They determine the quantity and quality of information obtained about a chemical, influence explicit and implicit assumptions used to analyze data, affect the way data are interpreted, and influence the weights used to combine disparate sets of data (see Ref. [17] for examples). This mix of science and policy can have undesirable effects on the quality of epidemiologic research by compromising the design, conduct, analysis, and interpretation of studies.

Adverse effects on the design and conduct of studies can occur in several ways. Political pressures to find quick answers to difficult questions have prompted poorly designed and hastily conducted investigations of possible danger from air pollutants and toxic wastes (e.g. Ref. [18]). The findings of such studies have been heavily criticized and the resulting controversies do not help the image of the field. Sometimes political pressures completely prevent a study. For example, an attempted county-wide investigation of the reproductive effects of aerial malathion spraying for the Mediterranean fruit fly was aborted because the hospital with the largest proportion of births declined to participate, due to the inflammatory political climate at the time [19]. Conversely, political pressures have initiated unwarranted studies virtually doomed to be inconclusive because of low, poorly documented exposures and lack of focus on specific disease entities. In the words of Doll [7]:

> "An epidemiological perspective starts not with the 10,000 chemicals that pollute a particular area, but with the 10,000 deaths that occur in that area each

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> year, and seeks to determine the major causes of those actual deaths. Such a perspective is much more likely to overlook a large number of small effects of various chemicals than laboratory science might be, but it is much less likely to overlook the chief determinants of current mortality rates and trends, especially if these are not simple direct effects of individual chemicals on molecular DNA".

Quality control and data analysis also are complicated by the political climate surrounding many studies of environmentally induced disease. The possibility of subjective reporting bias is increased, causing greater need for exposure and outcome validation [20]. For subjective disease assessments such as miscarriages and asthma attacks, there is need for difficult and expensive validation of negative outcomes among both exposed and unexposed populations.

Political pressures have their largest impact on the interpretation of epidemiologic data. Pressure to provide "bottom lines" produces quantitative risk estimates with spurious precision, numbers that, out of context, take on a life of their own. Such numbers are overinterpreted by laymen who expect a study to produce unequivocal answers, and when it does not, who criticize epidemiology for failing to achieve aims that go beyond available resources or methodologic capabilities.

Perhaps the most troubling impact of risk assessment activities concerns their side-effects for the epidemiologist. He has joined the ranks of psychiatrists, statisticians, and clinicians who take the stand as expert witnesseses in multimillion dollar lawsuits. While this activity helps keep bread on the table, one worries about the conflict between the one-sidedness of such an advocacy position and all of one's training to strive for a balanced perspective in weighing the strengths and limitations of a data set and placing it in the broader context of other data. Apart from the monetary inducements to take a unilateral view, there can also be pressures from peers and employers. Espousal of unpopular views may cost an epidemiologist invitations to conferences, permission by an employer to attend conferences [21], favorable reviews of papers, or even a job [22]. These hazards of course are not quite unique to the epidemiologist, but are shared by all those in the environmental health sciences whose work impinges on risk assessment for regulatory policy.

Equally worrisome is the tendency for political and philosophical differences to masquerade as scientific disputes. By now we have become inured to the familiar spectacle of government and industry epidemiologists aligning themselves in predictable camps in hassles over such issues as the incidence of brain tumors in the petrochemical industry [23], the fraction of U.S. cancer deaths attributable to occupational exposures [24], and the toxic importance of lead in automobile exhaust relative to that of lead in paint [25]. A second manifestation of this masquerade is the overkill in critiques of completed studies whose results have undesirable implications for the interests of one or another faction in a regulatory issue. While constructive peer review is a useful process, critiques that exaggerate a study's flaws and overlook its strengths for the purpose of discrediting its conclusions are counterproductive and a poor use of resources [26].

One can look back in history for more subtle and therefore perhaps more disturbing examples of how values influence scientific conclusions. Samuel George Morton was a 19th century self-styled "objective empiricist" who used his extensive collection of human skulls to study racial differences in cranial capacity, a putative marker for intelligence. His findings supported contemporary caucasian beliefs: whites above indians, blacks at the bottom. Stephen Jay Gould reanalyzed Morton's meticulously recorded raw data, and found a fabric of apparently unconscious manipulations in the form of errors, miscalculations and omissions, all in favor of white supremacy [27]. Gould notes that unconscious or dimly perceived finagling is probably endemic in science, since scientists are human beings rooted in political and cultural contexts. This example serves as a sobering reminder that reporting and interpreting one's data can require soul-searching, ruthless honesty, and courage.

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IV. THE FUTURE

It seems likely that public concern for environmental issues will not abate within this century, that public and corporate funds will continue to support research to monitor and evaluate environmental and occupational hazards to health, and that epidemiology will continue to play a critical role in this endeavor. It is therefore worthwhile to ask how regulators and epidemiologists can counteract the negative impacts of the political pressures endemic to regulation, and how epidemiologists and epidemiologic studies can provide guidance and support for the overall thrust of regulatory policy, as well as for the difficult decisions faced by regulators.

One antidote for the negative side effects of politicization on epidemiologic research is awareness of the hybrid nature of risk assessment activities. We need to recognize that a neat separation of regulatory policy into matters of fact and value is illusionary, and to sensitize ourselves to value judgements when they occur. They will and must occur, because setting standards for hazards at work and in the environment is a social and political process.

It is possible to abate political pressures by allocating sufficient funds, time and qualified personnel to the careful conduct of well designed studies, and by incorporating into the studies the advice of experts chosen to represent the concerns of all sides in sensitive issues. Recent investigations of pregnancy outcomes among women whose drinking water had been contaminated by a chemical leak from an underground tank at an electronics company provide a model for achieving such abatement. These investigations were conducted by the California Department of Health Services with the cooperation of the Santa Clara County Department of Health [32]. Before beginning the studies, the principal investigators formed an advisory committee of epidemiologists representing the interests of industry and of the citizens. The committee had a voice in the design, the data collection, the analyses and the interpretation of findings. The resulting consensus report provided a voice of reason that cooled many tempers in the heated political dispute surrounding the issues.

Epidemiologists can make their data more useful to regulators in several ways. A first step is good documentation. Clear, thorough and complete recording of the details and data that led to a study's conclusions are needed by regulatory scientists who must use the conclusions to formulate policy statements for public approval. The completeness of recording is important. Serfling [28] has decried the filtering of data and relevant research results that seem to contradict strongly held views about exposure effect, citing some occupational studies as examples. In 1981 the Interagency Regulatory Liaison Group published guidelines for documentation of epidemiologic studies [29, 30]. There now seems to be a consensus that these guidelines have been helpful in improving the clarity and completeness of study reports, and that they have not been the unwelcome intrusion of government agencies into epidemiologic turf feared by some.

Apart from the regulatory scientists' need for documentation of technical details and raw data, there is the layman's need for clear, nontechnical documentation of a study's conclusions, with particular emphasis on the degree of precision and sources of uncertainty associated with the conclusions. The policy decisions for which epidemiologic evidence is needed concern the public, and the public must make those decisions. Informed decisions by laymen require exposition of the major findings of a study, as well as the sources and nature of uncertainty about the findings in clear English without the use of esoteric jargon.

A second step to enhance the utility of epidemiologic data involves more even-handedness among epidemiologists about the strengths and weaknesses of a study, and less dredging for flaws with intent to discredit. It is imperative that scientists attempt to form a consensus about the interpretation of data, so that the courts are not forced to resolve technical scientific issues they are ill-equipped to handle. David L. Bazelon, Senior Court Judge of the U.S. Court of Appeals for the District of Columbia Court, complained that scientists cannot agree about the reliability of data, and that "... they disagree even more about the inferences to be drawn from the facts. Often, they can tell us only of 'the risk

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of risk'. . . . Courts must not be expected to resolve such questions. What judge knows enough to understand issues on the frontiers of nuclear physics, toxicology and other specialities informing health and safety regulations?" [31].

While it may be naive to think that epidemiologists can reach a consensus about uncertain data when millions of dollars and lives are at stake, there is no feasible alternative but to try to do so. The reproductive studies in Santa Clara County, and others like them, provide a paradigm for achieving such a consensus.

A third step to increase the utility of epidemiologic observations for risk assessment is aggressive monitoring of occupationally exposed populations. This is largely a job for industrial epidemiologists and occupational physicians, who should keep computerized, annually updated and linkable medical, job and smoking histories for all current (and to the extent feasible, former) employees. As noted by Doll [7], this monitoring makes sense from the industrial point of view, since most such studies would reveal no excess risk, and the accumulated negative human evidence, coupled with estimates of exposure levels for various agents, would be useful in resisting overzealous regulation. The monitoring also makes sense from the worker's point of view, because real hazards would be detected earlier than they otherwise might be. Finally, it makes sense for the public who would learn that prolonged exposure to quantified levels of many of the agents feared harmful have not produced observable human hazards.

The most promising developments in the monitoring of exposed populations involve the use of biological exposure markers in blood, tissue, urine, feces, hair or nail samples. Table 8 lists several of the markers detectable and quantifiable in human specimens. Such markers have the potential to document exposure levels, identify and quantify unusual susceptibility to environmental toxicants, detect precursors of injury or organ dysfunction, and provide etiologically supportive biological links between exposure and disease. Epidemiologic studies are needed to determine how well they correlate with exposure, and with preclinical or clinical manifestations of disease. They are also needed to determine the marker's reproducibility and persistence over time. Industrially exposed cohorts and cohorts of patients undergoing chemotherapy are ideal populations for such studies.

CONCLUSIONS

Epidemiology continues to play an indispensable role in risk assessment for regulatory purposes. Human data are needed to detect hazards missed by laboratory experiments, estimate exposure levels producing the highest socially acceptable risks, monitor changes in disease rates after the removal of putative causal agents, and provide a perspective for cost-effective allocation of public health resources.

Epidemiologists can make their data even more useful for risk assessment by providing clear and complete documentation for other scientists, and jargon-free documentation for those not versed in epidemiologic methods. Equally important is data interpretation with more balance and less factiousness. All of these objectives would be facilitated by the dialogue resulting from symposia, and from postdoctoral fellowships and visiting appointments allowing academic, regulatory and industrial epidemiologists to visit one another's worksites.

Occupationally exposed populations should be monitored for exposure levels, morbidity and mortality. Biological markers in human specimens promise to afford useful indices for exposures and for unusual susceptibility to exposures. There is need for work to correlate these markers with exposure history and with disease, and to establish their reproducibility, variability and persistence over time.

Risk assessment is both a political and a scientific process, and politicization will continue to complicate the conduct of epidemiologic research on the effects of environmental toxicants. Some restraint of political pressures can be achieved by allocating the funds and time for studies of high quality, with ongoing input from epidemiologists representing all interested parties.

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